

Suggestion for Master's thesis project collaboration between DTU Vet and Lundbeck

Aim: To investigate further the effect that urea- and MTU-conjugated dendrimers have on the formation and solubilization of fibrils formed by alpha-synuclein both in cell-free environments and in cell models.

Background: We have previously shown that urea- and MTU-conjugated dendrimers are able to clear cells from intracellular alpha-synuclein aggregates (we have also shown dendrimers to be able to clear prion-infected cells). Biochemically, we and others have shown that both unmodified and conjugated dendrimers can inhibit the fibrillation and in some cases dissolve pre-formed fibrils made from either alpha-synuclein or PrP106-126.

Methods:

- Biochemical assays:
 - o Western Blot
 - o Thioflavine T
 - o Electron microscopy (at CFIM, Panum)
 - o Other??
- Biological assays:
 - o Cell culturing
 - o Cytotoxicity assays
 - o Cellomics technology
 - o Confocal microscopy

The project would focus on two types of dendrimers; urea- and MTU-dendrimers, which both have a rather low cytotoxicity. The project will have initial focus on the biochemical assays – the biological assays will be run only on selected dendrimers. For the urea- and MTU-dendrimers, the cytotoxicity assays are completed, thus this will be run only in the case that other dendrimer types are included. We know that there is a difference in hydrophobicity between these two types of dendrimers, we would like to further explore how this impacts on the biological and biochemical effects of these, e.g. can we show if the dendrimers are being internalized into cells?

Supervisors:

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